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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,731	01/16/2004	Christopher J. Bond	11669.136USU1	6901

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EXAMINER	
GROSS, CHRISTOPHER M	
ART UNIT	PAPER NUMBER
1639	
MAIL DATE	DELIVERY MODE
03/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/759,731	BOND, CHRISTOPHER J.	
	Examiner	Art Unit	
	CHRISTOPHER M. GROSS	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *105-107,109-111,113 and 115-128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/30/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99 and 105-130.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99,108,112,129 and 130.

DETAILED ACTION

Responsive to communications entered 4/30/2007; 8/27/2007 and 12/12/2007. Claims 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99, 105-130 are pending. Claims 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99,108,112, 129,130 stand withdrawn. Claims 105-107, 109-111,113,115-128 are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Applicant's election of group I (Claims 1,3-7,9-12,15-16,22-24, 29-34,36-37,38-40,42, 44-46, 48-54, 59-60, 62-66, 68, 69-74,76, 96, 99; 2,18-21, 61,90-91,98; 105-114) and the species: a CDHR3 scaffold set forth in claims 105-114; N terminal sequence RIGR and C terminal sequence WVTW in the reply filed on 11/13/2006 is again acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-7,9-12,15,16,18-24,29-34,36-40,42,44-46,48-54,59-66,68-74,76,81-85,90-96,98,99 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/13/2006.

Claims 108,112,129,130 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/13/2006.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the prior application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Prods., Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994) [taken from MPEP 201.01]

The instant application, filed 1/16/2004 claims priority to provisional application 60/441,059 filed 01/16/2003 and claims benefit of provisional application 60/488,610 filed 07/18/2003 and claims benefit of provisional application 60/510,314 filed 10/08/2003.

Nevertheless, support for a CDRH3-phage coat fusion protein comprising a "N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" and a "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural" as set forth in amended claim 105 is not disclosed in the earlier applications. See also 35 USC 112 first paragraph considerations concerning new matter below.

Therefore 1/16/2004 is the date for the purposes of prior art concerning claims 105-107, 109-111,113,115-128.

Withdrawn Objection(s) and/or Rejection(s)

The rejection of claims 105 and 106 under 35 U.S.C. 102(b) as being anticipated by Spinelli et al (2000 Biochemistry 39:1217-1222) is hereby withdrawn in view of applicant's amendments to the claims.

The rejection of claims 105 and 106 under 35 U.S.C. 102(b) as being anticipated by Muyldermans et al (2001 TIBS 26:230-235) is hereby withdrawn in view of applicant's amendments to the claims.

The rejection of claims 105-114 under 35 U.S.C. 103(a) as being unpatentable over **La Rosa et al** (US Patent Application 2004/0123343) in view of either of **Spinelli et al** (2000 Biochemistry 39:1217-1222) **or Muyldermans et al** (2001 TIBS 26:230-235) is hereby withdrawn in view of applicant's amendments to the claims.

The provisional rejection of claims 105-114 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22 and 48 of copending Application No. 11/102502 in view of Spinelli et al (2000 Biochemistry 39:1217-1222) or Muyldermans et al (2001 TIBS 26:230-235) is hereby withdrawn in view of applicant's amendments to the claims.

New Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 105-107, 109,111,113,115-128 are rejected under 35 U.S.C. 102(a) as being anticipated by **Bond et al** (2003 J. Mol. Biol. 332:643-655 – IDS entry 9/27/2004).

This rejection is necessitated by Applicant's amendment to the claims.

The claimed subject matter per claim 105 is drawn to a fusion protein comprising:

at least a portion of a phage coat protein fused to a binding polypeptide comprising a CDRH3 scaffold comprising a N-terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural; and a C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural, and wherein the scaffold can accommodate the insertion of a central portion or loop of contiguous amino acids that can vary in sequence and in length.

Claims 106-107, 109,111,113,115-128 represent variations thereof.

Bond et al teach, through out the document and especially the abstract, structural contributions made by CDR3 loops in camelid V_HH domains.

Said CDR3 loops in camelid V_HH domains are taken as a CDRH3 scaffold, as set forth in claim 105 and defined in paragraph 0014 of the present published application (i.e. CDRH3 is the CDR3 of the heavy chain). Bond et al teach construction of a llama anti-human chorionic gonadotropin (alpha-HCG) V_HH fused to phage coat protein P3 on p 652, first paragraph. Bond et al teach in the paragraph bridging pp 644-645, the alpha-HCG structure comprises Trp 100 packing against Phe 37 and the aliphatic portion of Arg 45. Said Phe 37 and Arg 45 are taken as two structural amino acid positioned in the N terminal portion of claim 105. Said Trp 100 is taken as one structural

amino acid positioned in the C terminal portion of claim 105. Bond et al teach on p 645 last paragraph insertions into said alpha-HCG at the short seven residue CDR3 loop, therein accommodating insertion of a central portion, as set forth in claim 105.

Bond et al teach in figure 1, camelid V_HH domains may comprise a disulfide bond between residues Cys 33 and Cys 109, reading on claim 106.

Bond et al teach in table 4a, a V_HH bearing a 17 residue insert comprising the sequence RIGR-...-WVTW (elected species) as an insert, reading on: R-L/I/MA_3-R when A_3 is Gly, as set forth in claim 107; the R-I of claim 109; the W-V of claim 111; C terminal portion being 4 amino acids of claim 113; R-L/I/MA_3-R when A_3 is Gly and W-A7-A8-A9-A10-A11, wherein A7-11 can be any amino acid as set forth in claim 115.

Bond et al teach on p 649 second paragraph and figure 3b, shotgun alanine scanning as indicative of RI and WV being structural in said RIGR...WVTW insert, as set forth in claim 116-120.

Said WV is in positions 100i and 100j, according to figure 4a of Bond et al, as set forth in claim 121.

Bond et al teach in the paragraph bridging the left and right column on p 652 that *individual* clones were sequenced. The examiner submits that individual clones, being identical, inherently comprise non-random codon sets, such as set forth in claim 122.

Said Phe 37 reads on the phenylalanine of claim 124. Said Arg 45 reads on the arginine of claim 125. Bond et al teach Threonine at position 91 in figure 2, reading on claim 126.

Said RIGR-...WVTW insert of Bond et al in figure 4a is 17 residues and reads on claim 128 when A1 is R, A2 is I, A3 is G, A4 is R, n is 9, A6 is S, A7 is W, A8 is V, A9 is T and A10 is W.

New Claim Rejection(s) – 35 USC § 112

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 105-107, 109-111,113,115-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "new matter" rejection.

This rejection is necessitated by Applicant's amendment to the claims.

Claim 105 has been amended to insert the limitations concerning a fusion protein comprising a CDRH3 scaffold plus at least a portion of a phage coat protein bearing a "N terminal portion of about 1 to 4 amino acids in which some or all of the amino acid positions are structural" and "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural"

The specification as originally filed provided no implicit or explicit support for CDRH3-phage coat ***fusion*** proteins with structural limitations regarding particular

sequence positions (i.e. N vs. C terminus) and/or numbers (1 to 4 or 1 to 6) of structural amino acids.

Additionally, the specification as originally filed provided no implicit or explicit support for any species of CDRH3-phage coat ***fusion*** protein bearing a C terminal sequence CWVTW, as set forth in claim 110.

Applicants are reminded that it is their burden to show where the specification supports any amendments to the disclosure. See MPEP 714.02, paragraph 5, last sentence and also MPEP 2163.06 I.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure.*

The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 123-126,127 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is necessitated by Applicant's amendment to the claims.

Claim 123 recites the limitation "the binding polypeptide" in line 1. There is insufficient antecedent basis for this limitation in the claim.

As currently written, the metes and bounds of the claims are unascertainable. Therefore, claim 123 and all dependent claims are rejected under 35 USC 112, second paragraph.

The term "variant amino acid" in claim 123 line 3 represents vague and indefinite language because it is not clear how *one* fusion protein per claim 105, from which claim 123 depends, may have different residues at positions 37,45 and 91. For example, the examiner submits, in using 20 of the common amino acids, varying just one position (e.g. 91), would generate for 20 *different* fusion proteins rather than *a* fusion protein as set forth in claim 105.

Therefore, claim 123 and all dependent claims are rejected under 35 USC 112, second paragraph.

The term "variants thereof" in claim 127 is a relative term which renders the claim indefinite. The term "variant" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Here, it is not clear

if the variation concerns chimera composed of the viral coat proteins p3,p8,Soc, Hoc, 9pD and pV1 or else if the variation is with regard to the primary sequence of *each* of said proteins separately.

Claim 127 recites vague and indefinite language coat protein "pV1." It appears pV1 is represents typographical error, which should read "pVI," however the specification does not provide a definition for "pV1" and in accordance with MPEP 2173.02: If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate. See Morton Int 'l, Inc. v. Cardinal Chem. Co., 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993).

New Double Patenting Rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 105,107, 109,111,113,115-122,127-128 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22, 25,26,30,31,35-37,48-50 of copending Application No. 11/102502 (referred to as '502) in view of **Sidhu et al** (2000 J. Mol. Biol. 296:487-495 – IDS entry 9/27/2004) and evidenced by Bond et al (2003 J. Mol. Biol. 332:643-655 – IDS entry 9/27/2004).

This rejection is necessitated by Applicant's amendment to the claims.

Overlapping and Similar Embodiments

Although the conflicting claims are not identical, they are not patently distinct from each other because, for example, claims 105,107,109,111,113,115-120,128-129 represent structural variants of all that is recited in claims 22, 25, 26,30, 48, 50 of '502 or, alternatively overlap in scope to a large extent and, as a result, the overlapping claims would be rendered obvious.

For **claim 105**, the '502 application claims a coat protein fusion protein (e.g. see claims 35,36)

For **claim 127**, the '502 application claims viral coat proteins pIII, pVIII, Soc, Hoc, 9pD, PVI and variants thereof (e.g. see claim 37).

For **claim 121**, the '502 application claims structural amino acids at positions 100i, 100j, and 100h (e.g. see claim 49).

For **claim 122**, the '502 application claims a non-random codon set (e.g. see claim 31).

Additionally, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify embodiments of '502 that fall outside the scope of the present application to select a specifically disclosed embodiment that falls within the scope of the present application because these embodiments describe immunoglobulins with similar physiochemical properties in that they all possess a common core structure and/or activity. For instance, claim 22 of application 11/102,502 is drawn to a plurality of antibody variable domains, wherein each antibody variable domain comprises a variable framework region (VFR). Said "VFR" refers to framework residues that form a part of the antigen binding pocket or groove and/or that may contact antigen, as defined by paragraph 0043 of the 11/102,502 published application. The examiner submits that CDRH3 of the present invention is part of an antigen binding pocket, especially as evidenced by Bond et al figure 1.

Application '502 differs from the presently examined fusion protein in being drawn to a plurality of VFRs.

Sidhu et al teach, throughout the document and especially the abstract, preparation of a library (plurality) of human growth hormone variants as fusion proteins with phage coat protein VIII.

One would have been motivated to prepare a plurality CDR3 scaffold fusion proteins (e.g. VFRs) with phage coat protein VIII like Sidhu because it would have enabled one to detect the best binding variant with 100 fold better sensitivity, as noted by Sidhu et al in the abstract line 7 and the right column on p 487 first full paragraph lines 8-10.

Furthermore, one of ordinary skill in the art would have been further motivated to make such a modification because such modifications are disclosed as "preferred" since the dependent claims of the '502 application "teach toward" Applicant's claimed fusion protein (e.g. see claim 35-37 concerning VFR phage fusion proteins; see claim 30 directed toward a central portion no more than 20 amino acids, as reflected in claims 107 and 111 of applicant's presently claimed materials or see claim 50 directed toward a VFR including a RI...WVTW sequence; see claim 48 directed to a CDR3 domain)

This is a provisional obviousness-type double patenting rejection.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on 571 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M Gross
Examiner
Art Unit 1639

cg

/Mark L. Shibuya, Ph.D./
Primary Examiner, Art Unit 1639